REMARKS/ARGUMENTS

In response to the Final Rejection mailed February 10, 2006, applicants present the following clarifying remarks.

Claim 60 was rejected under 35 USC 112, second paragraph as being considered vague and indefinite by reciting "allowing the vector to spread throughout the plant before recovering the polypeptide." The examiner presents two questions as to alternative meanings. The answer is yes to both! The vector does spread throughout the plant including the roots, stems, etc. in the specification's working Examples. Also, the polypeptide is recovered from the leaves as is recited in independent claim 51, step (e) from which claim 60 depends. These two answers are not mutually exclusive as the rejection implies because the recited language in claim 60 uses the word "before" to indicate where the claim 60 "step" appears in the sequence order of the method of claim 51. Accordingly, the rejection should be withdrawn.

Claim 60 was rejected under 35 USC 112, first paragraph as containing new matter in the phrase "allowing the vector to spread throughout the plant before recovering the polypeptide." Actually, this "step" in the method is supported in several locations in the specification such as before "general references" in paragraph 76, also paragraphs 217, 220, 231 and Example 4. Also see paragraph 324 for symptoms of systemic infection in the plants. Since the systemic spread of Tobacco Mosaic Virus in plants is well known to occur, and because polypeptide is recovered from the interstitial fluid in the working examples, systemic spread has already occurred. Accordingly, the rejection should be withdrawn.

Claims 51-60 were rejected under 35 USC 103 as being unpatentable over Hawkins et al, Fiedler et al, Caspar et al, Tang et al and Hakim et al. The rejection is essentially the same as previously. This rejection is respectfully traversed.

The present claims recite several features not taught or suggested by any combination of the above references. Any one of these features is sufficient to negate the rejection. Many of these were presented before, and applicants disagree with the examiner. However the following 5 points are limited to issues where the examiner is clearly misreading the claims or the prior art and thus the dispute is factual not a difference of opinion.

1) Claim 51 step (c) recites "incorporating ... constructs into a transient plant expression vector". None of the references disclose a "transient plant expression vector". The examiner points to Fiedler et al but the vectors used therein produce plants with transgenic progeny. Fiedler et al uses second-generation transgenic plants for extracting the scFv polypeptide. Such second-generation plants have always contained the foreign gene and therefore cannot be considered having the foreign gene in a "transient" vector. Further, second generation transgenic plants were not be produced by "transfecting a plant with the vector" as recited in claim 51, step (d).

The examiner has stated, "Fiedler et al does teach the transient expression of plants for the production of scFv..." This is not the claimed recitation of "incorporating ... constructs into a transient plant expression vector" or the claimed recitation of "transfecting a plant with the vector". The claim recites the presence of the vector (a nucleic acid containing composition) as being "transient" in the plant cell. Whether or not Fiedler et al has a "transient" process for making scFv (a polypeptide compound) is not the same or even suggestive of the claimed method. Accordingly, the rejection should be withdrawn.

2) The claims do NOT recite producing any polypeptide but only those having the proper "correctly-folded" property. This is worded in the claims as:

Claim 51 - "recovering the polypeptide as a soluble correctly-folded protein",

Claim 52 - "induces an idiotype-specific immune response",

Claim 54 - "correct folding of said polypeptide to mimic the tumor epitope in its native form in or on said tumor cell", and

Claim 58 - "the polypeptide induces the idiotype-specific immune response without a need for an adjuvant or other immunostimulatory material".

None of the references produce a "correctly-folded" polypeptide and evidence already of record establishes that the linker approaches used by each reference either do not work or are not designed to produce the claimed polypeptide. Applicants do not claim all polypeptides with a common domain-linker-domain configuration; rather, applicants claim only those with the resulting properties claimed.

The scFv polypeptide with the (GGGGS)3 linker of Caspar et al and Hawkins et al, and Hakim et al does not result in a "correctly-folded protein" because it does not "induce an idiotype specific immune response" that "mimics the tumor epitope" "without a need for an adjuvant or other immunostimulatory material". Claim language in quotes. The examiner's speculation that the prior art compositions may have the claimed properties is contradicted by the prior art of record. Hakim et al prepared the scFv with the (GGGGS)3. See Figure 1, first construct. It did not work because when the protein was used for vaccination, no IgG was induced. See Table II. It did not work because the protein vaccination was completely ineffective with an identical survival time as negative control mice when challenged with tumor cells. See Figure 5. The fact that the references try adding adjuvants, immunostimulatory materials, strong antigens to the polypeptide or try using nucleic acid-based vaccines in order to obtain an appropriate vaccination is further evidence that the basic design does not work.

The claimed polypeptide, which resembles a scFv (with a different linker), does work and has the claimed properties of a correctly folded protein. An approach that does

not work is a strong negative teaching against any such polypeptide having the claimed properties.

The scFv with the (GGGGS)3 linker of Fiedler et al may produce a molecule with certain binding properties but Fiedler et al is silent as to its vaccine properties. From Hakim et al, it would not be expected to mimic the epitope with a correctly folded protein. Also, from Hakim et al it is clear that binding ability alone is not sufficient. See Hakim et al where the ineffective scFv were used for binding purposes in immunoassays and a Western blot assay. Therefore, there is no presumption (and considerable contrary evidence) that the Fiedler et al scFv would be correctly folded for the purposes of the present invention.

The scFv-like binding molecules in Tang et al were made with various linkers to enhance binding properties over the natural configuration. While this is very desirable to produce superior binding agents, it involves making the molecule less native than the natural molecule and therefore even less correctly folded for vaccine purposes. As mentioned above the goal the claimed invention is to mimic a native form for obtaining an immune response against the tumor. Tang et al's goal is to make the polypeptide less native by forming it differently to increase its binding properties.

Since none of the references can show any polypeptide with the claimed properties, it would not be obvious to prepare the claimed polypeptide by the claimed method.

3) Claims 54-57 recite using a library of linkers. The linkers in the library have certain limitations. Tang et al also has a library of linkers but the limitations on the linkers are different. The examiner has contended that a common linker in both libraries is possible. There is no suggestion or motivation to prepare the claimed library. While the two libraries may have some linkers in common as their properties have a small amount of overlap, this issue is peripheral to the claims.

These claims are methods for using a library of linkers for a particular purpose. As stated above, Tang et al is using their library of linkers to produce a different type of product (a superior binding agent) from the product made by the present invention (a vaccine). Compounds are not being claimed but rather methods for using a library. Even if a particular member of the two libraries may be the same, the use of the respective linker libraries in different methods is different. For the present method claims, there is no motivation to use the linker library in Tang et al and therefore the rejection should be withdrawn.

4) Claim 59 recites, "the vector is transiently expressed in the cytoplasm." This refers to the cytoplasm of the plants from which the polypeptide is recovered. The only reference applied to the rejection involving producing anything in plants is Fiedler et al. They recover polypeptides from second-generation transgenic plants where the vector is present in the nucleus NOT present in the cytoplasm.

Fiedler et al, page 208 section 2.2 states "The plasmids were transferred into the Agrobacterium tumefaciens strain pGV2260 [26] by electroporation and used for leaf disc transformation [27] of Nicotiana tobaccum cv. SNN." [26] refers to Deblaere et al, Nucleic Acids Res. 985 Jul 11;13(13):4777-88. This vector integrates into the genome of the tobacco cells. Thus, the vector is permanently in the cell's nucleus of any regenerated plant selected to produce the polypeptide.

With Fiedler et al having their scFv gene in the nucleus, they do not teach a vector in the cytoplasm and therefore the rejection should be withdrawn.

5) Claim 60 recites, "allowing the vector to spread throughout the plant". The vectors used by Fiedler et al do not spread throughout the plant. The other references applied do not even use plants. Therefore, none of the references suggest allowing this to happen and accordingly the rejection should be withdrawn.

In view of the above amendments and comments, the claims are now in conditions for allowance and applicants request a timely Notice of Allowance be issued in this application.

If needed, applicants petition for sufficient extension of time for consideration of this paper.

The commissioner hereby is authorized to charge payment of any fees, including extension of time fees, under 37 CFR § 1.17, which may become due in connection with the instant application or credit any overpayment to Deposit Account No.500933.

Respectfully submitted,

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